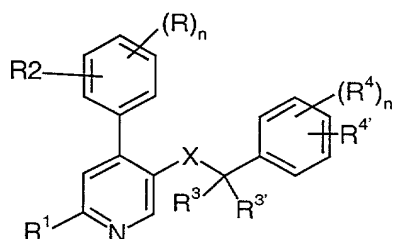


Claims:

1. A compound of the formula



wherein

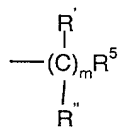
R is hydrogen or halogen;

R¹ is $-(C\equiv C)_mR^{1'}$ or $-(CR'=CR'')_mR^{1'}$

wherein R^{1'} is

a) hydrogen or halogen,

b) cyano, or the following groups:



c) ,

d) $-C(O)NR'R''$,

e) $-C(O)O(CH_2)_mR^5$,

f) $-C(O)R^5$,

g) $-N(OH)-(CH_2)_mR^5$,

h) $-NR'C(O)-(CH_2)_mR^5$,

i) $-N[C(O)-R']_2$,

j) $-OR^6$,

k) $-(CH_2)_m-SR^6$, $-(CH_2)_m-S(O)R^6$, or $-(CH_2)_m-S(O)_2R^6$,

l) aryl, unsubstituted or substituted by one or more substituents, selected from halogen,

trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro,

$-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

m) is a five or six membered aromatic heterocycle, containing one to four heteroatoms,

selected from N, O or S and, unsubstituted or substituted by one or more

substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)OR'$, $-C(O)NR'R''$ or $-C(O)R'$, n) is a five or six membered non-aromatic heterocycle of the formula



which may contain one additional heteroatom, selected from N, O or S,

R'/R'' are hydrogen, hydroxy, lower alkyl, cycloalkyl

or aryl, wherein the lower alkyl, cycloalkyl or aryl group is unsubstituted or substituted by at least one substituent, selected from halogen,

trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'''R''''$, nitro,

$-(CH_2)_nOR'''$, $-C(O)NR'''R''''$, $-C(O)OR'''$ or $-C(O)R'''$,

R'''/R'''' are independently from each other hydrogen, lower alkyl, cycloalkyl or aryl,

R^5 is hydrogen, cyano, hydroxy, halogen, trifluoromethyl, $-C(O)OR'$, $-OC(O)R'$ or aryl, unsubstituted or substituted at least one substituent, selected from halogen,

trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro,

$-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$, or is a five or six membered

heteroaryl group, containing one to four heteroatoms, selected from N, O or S,

unsubstituted or substituted by at least one substituent, selected from

halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro,

$-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

R^6 is hydrogen, lower alkyl, trifluoromethyl, or aryl, wherein the lower alkyl or aryl group is unsubstituted or substituted by at least one substituent, selected from

halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro,

$-C(O)NR'R''$, $-(CH_2)_nOR'$, $-C(O)OR'$ or $-C(O)R'$, or is a five or six membered

heteroaryl group, containing one to four heteroatoms, selected from N, O or S and

is unsubstituted or substituted by at least one substituent, selected from halogen,

trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro,

$-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

R^7 is $-C(O)-(CH_2)_mOH$ or an oxo group;

R^2 is hydrogen, lower alkyl, lower alkoxy, halogen or CF_3 ;

$R^3/R^{3'}$ are hydrogen, lower alkyl or form together with the carbon atom to which they are attached a cycloalkyl group;

$R^4/R^{4'}$ are hydrogen, halogen, CF_3 , lower alkyl or lower alkoxy;

R and R^2 or R^4 and R^4' may be together $-CH=CH-CH=CH-$, unsubstituted or substituted by one or two substituents selected from lower alkyl, halogen or lower alkoxy;

X is $-C(O)N(R^8)-$, $(CH_2)_pO-$, $-(CH_2)_pN(R^8)-$, $-N(R^8)C(O)-$ or $-N(R^8)-(CH_2)_p-$; wherein R^8 is hydrogen or lower alkyl;

n is 1 or 2;

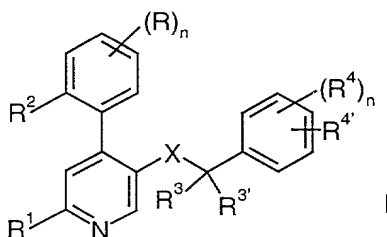
m is 0, 1, 2, 3 or 4;

o is 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable acid addition salt thereof.

2. A compound of the formula



wherein

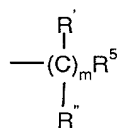
R is hydrogen or halogen;

R^1 is $-(C\equiv C)_mR^{1'}$ or $-(CR'=CR'')_mR^{1'}$

wherein $R^{1'}$ is

a) halogen,

b) cyano, or the following groups:



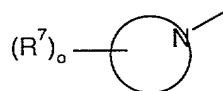
c) ,

d) $-C(O)NR'R''$,

e) $-C(O)O(CH_2)_mR^5$,

f) $-C(O)R^5$,

- g) $-N(OH)-(CH_2)_mR^5$,
h) $-NR'C(O)-(CH_2)_mR^5$,
i) $-N[C(O)-R']_2$,
j) $-OR^6$,
k) $-SR^6$, $-S(O)R^6$, or $-S(O)_2R^6$,
l) aryl, unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,
m) is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and is unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)OR'$, $-C(O)NR'R''$ or $-C(O)R'$,
n) is a five or six membered non-aromatic heterocycle of the formula



or a five or six membered non-aromatic heterocycle containing one additional heteroatom, selected from N, O or S,
 R'/R'' are hydrogen, lower alkyl, cycloalkyl or aryl,
unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'''R''''$, nitro, $-(CH_2)_nOR'''$, $-C(O)NR'''R''''$, $-C(O)OR'''$ or $-C(O)R'''$,
 R'''/R'''' are independently from each other hydrogen, lower alkyl, cycloalkyl or aryl,
 R^5 is hydrogen, cyano, hydroxy, halogen, trifluoromethyl, $-C(O)OR'$ or aryl,
unsubstituted or substituted by at least one substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$, or is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and is unsubstituted or substituted by at least one substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,
 R^6 is hydrogen, lower alkyl, trifluoromethyl, or aryl,
unsubstituted or substituted by at least one substituents, selected from halogen,

trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-C(O)NR'R''$, $-(CH_2)_nOR'$, $-C(O)OR'$ or $-C(O)R'$, or is a five or six membered heteroaryl group, containing one to four heteroatoms, selected from N, O or S and is unsubstituted or substituted by at least one substituent, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)NR'R''$, $-C(O)OR'$ or $-C(O)R'$,

R^7 is $-C(O)-(CH_2)_mOH$ or an oxo group;

R^2 is hydrogen, lower alkyl, lower alkoxy, halogen or CF_3 ;

$R^3/R^{3'}$ are hydrogen, lower alkyl or form together with the carbon atom to which they are attached a cycloalkyl group;

$R^4/R^{4'}$ are hydrogen, halogen, CF_3 , lower alkyl or lower alkoxy;

R and R^2 or R^4 and $R^{4'}$ may be together $-CH=CH-CH=CH-$, unsubstituted or substituted by one or two substituents selected from lower alkyl, halogen or lower alkoxy;

X is $-C(O)N(R^8)-$, $(CH_2)_pO-$, $-(CH_2)_pN(R^8)-$, $-N(R^8)C(O)-$ or $-N(R^8)-(CH_2)_p-$; wherein R^8 is hydrogen or lower alkyl;

n is 1 or 2;

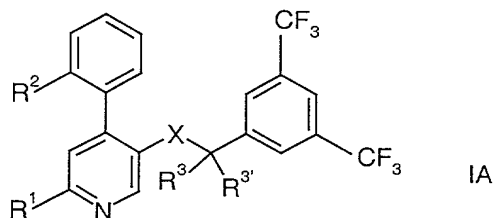
m is 0 to 4;

o is 1 or 2; and

p is 1 or 2;

or a pharmaceutically acceptable acid addition salt thereof.

3. A compound of formula IA according to claim 1,



wherein

R^1 is halogen, $-(CH_2)_mCN$, $-C(O)O$ -lower alkyl, $-(CH_2)_mOH$, $-N(OH)(CH_2)_mOH$, $-N(R)C(O)-(CH_2)_mOC(O)$ -lower alkyl,

-N[C(O)-cycloalkyl]₂, -N(R)C(O)-(CH₂)_mOH, pyridin-2,3,4-yl or phenyl, unsubstituted or substituted by lower alkyl, lower alkoxy or hydroxy or is morpholinyl or piperazinyl, substituted by -C(O)-(CH₂)_mOH or oxy group(s),

R is hydrogen or lower alkyl;

R² is lower alkyl or halogen;

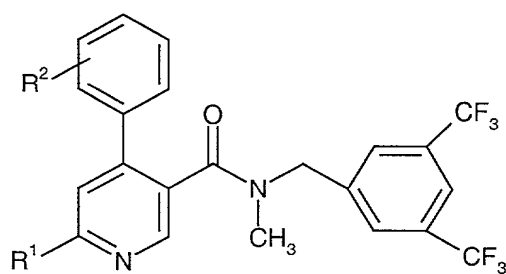
R³/R^{3'} are hydrogen or lower alkyl;

X is -C(O)N(R⁸)- or -N(R⁸)C(O)-;

R⁸ is hydrogen or lower alkyl; and

m is 1 or 2.

4. A compound according to claim 1 having the formula



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wherein R¹ and R² are as defined above.

5. A compound according to claim 4, further comprising R² being lower alkyl.

6. A compound according to claim 5 further comprising R² being 2-methyl.

7. A compound according to claim 6 further comprising R¹ being an unsubstituted or substituted five or six membered non-aromatic heterocycle containing at least one nitrogen or one nitrogen and one additional hetero atom selected from the group N, O or S.

8. A compound according to claim 7 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-hydroxyacetyl-piperazin-1-yl)-N-methyl-4-o-tolyl-nicotinamide.

9. A compound according to claim 7 wherein the compound is 4-o-tolyl-1',2',3',6'-tetrahydro-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
10. A compound according to claim 6 further comprising R^1 being aryl substituted by at least one substituent.
11. A compound according to claim 10 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-methoxy-phenyl)-N-methyl-4-o-tolyl-nicotinamide.
12. A compound according to claim 10 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(4-hydroxymethyl-phenyl)-N-methyl-4-o-tolyl-nicotinamide.
13. A compound according to claim 6 further comprising R^1 being a five or six member hetero aryl group containing one to four heteroatoms substituted by at least one substituent.
14. A compound according to claim 13 wherein the compound is 2'-methyl-4-o-tolyl-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
15. A compound according to claim 13 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(3-methyl-[1,2,4]oxadiazol-5-yl)-4-o-tolyl-nicotinamide
16. A compound according to claim 6 further comprising R^1 being unsubstituted hetero aryl.
17. A compound according to claim 16 wherein the compound is 4-o-tolyl-[2,4']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
18. A compound according to claim 16 wherein the compound is 4-o-tolyl-[2,3']bipyridinyl-5-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide.
19. A compound according to claim 6 further comprising R^1 being cyano.
20. A compound according to claim 19 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-cyanomethyl-N-methyl-4-o-tolyl-nicotinamide.
21. A compound according to claim 6 further comprising R^1 being $-(CH_2)_m-S(O)R^6$.

22. A compound according to claim 21 wherein the compound is (RS)-N-(3,5-bis-trifluoromethyl-benzyl)-6-(2-hydroxy-ethanesulfinylmethyl)-N-methyl-4-o-tolyl-nicotinamide.

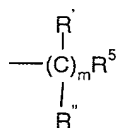
23. A compound according to claim 21 wherein the compound is (RS)-N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(pyridine-2-sulfinyl)-4-o-tolyl-nicotinamide.

24. A compound according to claim 6 further comprising R^1 being $-OR^6$.

25. A compound according to claim 24 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-hydroxymethyl-N-methyl-4-o-tolyl-nicotinamide.

26. A compound according to claim 24 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(3-hydroxy-propoxy)-N-methyl-4-o-tolyl-nicotinamide.

27. A compound according to claim 6 further comprising R^1 being



wherein R' , R'' , R^5 and m are as above.

28. A compound according to claim 27 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-(3-cyano-propyl)-N-methyl-4-o-tolyl-nicotinamide.

29. A compound according to claim 6 further comprising R^1 being $-(CH_2)_m-SR^6$, and m is as above.

30. A compound according to claim 29 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(1-methyl-1H-imidazol-2-ylsulfanylmethyl)-4-o-tolyl-nicotinamide.

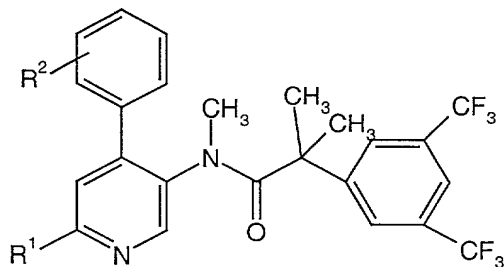
31. A compound according to claim 6 further comprising R^1 being $-(CH_2)_m-S(O)_2R^6$, with m and R^6 as above.

32. A compound according to claim 31 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-N-methyl-6-(pyridine-2-sulfonyl)-4-o-tolyl-nicotinamide.

33. A compound according to claim 4 further comprising R^1 and R^2 being halogen.

34. A compound according to claim 33 wherein the compound is N-(3,5-bis-trifluoromethyl-benzyl)-6-chloro-4-(4-fluoro-phenyl)-N-methyl-nicotinamide.

35. A compound according to claim 1 having the structure



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wherein R^1 and R^2 are as above.

36. A compound according to claim 35 further comprising R^1 being halogen.

37. A compound according to claim 36 wherein said halogen is chlorine.

38. A compound according to claim 37 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-chloro-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide.

39. A compound according to claim 35 further comprising R^2 being halogen.

40. A compound according to claim 39 wherein said halogen is 2-chloro.

41. A compound according to claim 40 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-{4-(2-chloro-phenyl)-6-[hydroxy-(2-hydroxy-ethyl)-amino]-pyridin-3-yl}-N-methyl-isobutyramide.
42. A compound according to claim 40 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-6-(3-oxo-morpholin-4-yl)-pyridin-3-yl]-N-methyl-isobutyramide.
43. A compound according to claim 40 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[4-(2-chloro-phenyl)-2'-methyl-[2,4']bipyridinyl-5-yl]-N-methyl-isobutyramide.
44. A compound according to claim 35 further comprising R^2 being lower alkyl.
45. A compound according to claim 44 wherein R^2 is methyl.
46. A compound according to claim 45 wherein R^1 is $-NR'C(O)-(CH_2)_mR^5$ and R' , R^5 and m are as above.
47. A compound according to claim 46 wherein the compound is acetic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-ylcarbamoyl)-methyl ester.
48. A compound according to claim 46 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2-hydroxy-acetylamino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.
49. A compound according to claim 46 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(hydroxyacetyl-methyl-amino)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.
50. A compound according to claim 45 further comprising R^1 being a five or six membered non-aromatic heterocycle of the formula



or a five or six membered non-aromatic heterocycle containing one additional heteroatom, selected from N, O or S and wherein R^7 and o are as above.

51. A compound according to claim 50 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(2,5-dioxo-pyrrolidin-1-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.

52. A compound according to claim 50 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(3-oxo-morpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-isobutyramide.

53. A compound according to claim 45 further comprising R^1 being $-N[C(O)-R']_2$ and wherein R' is as above.

54. A compound according to claim 53 wherein the compound is cyclopropanecarboxylic acid (5-{[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino}-4-o-tolyl-pyridin-2-yl)-cyclopropanecarbonyl-amide.

55. A compound according to claim 45 further comprising R^1 being $-N(OH)-(CH_2)_mR^5$, wherein R' , m and R^5 are as above.

56. A compound according to claim 55 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-{6-[hydroxy-(2-hydroxy-ethyl)-amino]-4-o-tolyl-pyridin-3-yl}-N-methyl-isobutyramide.

57. A compound according to claim 45 further comprising R^1 being $-(C\equiv C)_mR^{1'}$ and wherein m and $R^{1'}$ are as above.

58. A compound according to claim 57 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-ethynyl-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide.

59. A compound according to claim 57 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxy-prop-1-ynyl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.

60. A compound according to claim 45 further comprising R^1 being $-C(O)O(CH_2)_mR^5$ and wherein m and R^5 are as above.

61. A compound according to claim 60 wherein the compound is 5-[[2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl]-methyl-amino]-4-o-tolyl-pyridine-2-carboxylic acid methyl ester.

62. A compound according to claim 45 further comprising R^1 being $-OR^6$ and wherein R^6 is as defined above.

63. A compound according to claim 62 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-(6-hydroxy-4-o-tolyl-pyridin-3-yl)-N-methyl-isobutyramide.

64. A compound according to claim 45 further comprising R^1 being $-(CH_2)_m-S(O)R^6$ and wherein m and R^6 are as defined above.

65. A compound according to claim 64 wherein the compound is (RS)-2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-methoxy-benzenesulfinyl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.

66. A compound according to claim 45 further comprising R^1 being a five or six membered aromatic heterocycle, containing one to four heteroatoms, selected from N, O or S and, unsubstituted or substituted by one or more substituents, selected from halogen, trifluoromethyl, lower alkyl, lower alkoxy, cyano, hydroxy, $-NR'R''$, nitro, $-(CH_2)_nOR'$, $-C(O)OR'$, $-C(O)NR'R''$ or $-C(O)R'$, and wherein n, R' and R'' are as above.

67. A compound according to claim 67 wherein the compound is 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(3-hydroxymethyl-isoxazol-5-yl)-4-o-tolyl-pyridin-3-yl]-N-methyl-isobutyramide.

68. A method of alleviating the symptoms of patient having a disease state treatable by modulation of NK-1 receptor antagonists comprising administering an effective amount of a medicament containing a sufficient quantity of the compound of claim 1.

69. A medicament containing a compound of claim 1 and at least one pharmaceutically acceptable excipient

70. A medicament according to claim 69 for the treatment of diseases related to NK-1 receptor antagonists.
